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(21) International Application Number: PCT/US92/05877 (22) International Filing Date: 14 July 1992 (14.07.92) (30) Priority data: PCT/US91/04979 15 July 1991 (15.07.91) WO (34) Country for which the regional or international application was filed: US (71) Applicant (for all designated States except US): MINNTECH CORPORATION [US/US]; 14605 28th Avenue North, Minneapolis, MN 55447 (US). (72) Inventors; and (75) Inventors/Applicants (for US only) : COSENTINO, Louis, C. [US/US]; 2435 Holly Lane, Plymouth, MN 55447 (US). JANSEN, Walter, B. [US/US]; 4015 Evergreen Lane, Plymouth, MN 55441 (US). HALL, Robert, T., II [US/US]; 20175 Rhoda Avenue, Welch, MN 55089 (US). MARINO, Rosario, M. [CO/US]; 4847 Westgate Road, Minnetonka, MN 55345 (US). HALL, Kimberly, L. [US/US]; 20175 Rhoda Avenue, Wlch, MN 55089 (US).	(74) Agent: WRIGLEY, Barbara, A.; Minntech Corporation; 14605 28th Avenue North, Minneapolis, MN 55447 (US). (81) Designated States: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG). Published <i>With international search report.</i>	
(54) Title: STABLE, ANTICORROSIVE PERACETIC/PEROXIDE STERILANT (57) Abstract Stable microbicides comprising hydrogen peroxide, peracetic acid, acetic acid and purified water substantially free of contaminants, sequestrants or stabilizers and having anticorrosive properties for metals used in surgical and dental instruments is disclosed.		

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1 **STABLE, ANTICORROSIVE PERACETIC/PEROXIDE STERILANT**2 Background of the Invention3 1. Field of the Invention

4 This invention relates generally to the field of
5 microbicides. In particular, it relates to a stable microbicide
6 having anticorrosive properties comprising a mixture of hydrogen
7 peroxide, peracetic acid, acetic acid and purified water which
8 is substantially free of contaminants or stabilizing and
9 sequestrant type additives.

10 2. Description of the Related Art

11 Peracetic acid/peroxide containing compositions have a
12 long history of use as disinfectants and sterilizers due to
13 their microbicidal activities. However, peroxide containing
14 compositions are high-energy-state compounds and as such can be
15 considered thermodynamically unstable. Therefore, because there
16 is a strong tendency for these compositions to decompose in the
17 presence of multivalent metal ions, stabilizers are added.
18 Stabilizers may be agents such as sodium pyrophosphate,
19 phosphonic acid or chelating agents such as 8-hydroxyquinoline.
20 Stabilizers act by removing trace metals which accelerate the
21 decomposition of peroxides. Stabilizers also accelerate the
22 reaction between hydrogen peroxide and acetic acid to form
23 peracetic acid. Therefore, for any given concentration of
24 hydrogen peroxide and acetic acid, the addition of a stabilizer
25 increases the concentration at equilibrium of peracetic acid.

26 While conventional art compositions are stable due to
27 the use of added stabilizers, they are also highly corrosive to
28 the very metals they are designed to disinfect namely surgical
29 and dental instruments made of aluminum or brass, which
30 instruments are often plated with an ornamental or protective
31 layer of nickel or nickel and/or chromium. Additionally,
32 certain susceptible individuals often exhibit allergic reactions
33 to the conventional art formulations. Further, after prolonged
34 use these conventional art formulations often leave mineral-like
35 deposits on the metal instruments they sterilize.

36

1 A concentrated composition that contains no stabilizer
2 or sequestrant type additives that is both stable during storage
3 for prolonged periods of time and possesses anticorrosive
4 properties would be a decided advantage over these conventional
5 formulations. Further, a use-dilution formulation that may be
6 reused several times, is stable for relatively long periods in
7 the diluted form and possesses anticorrosive properties would be
8 a further advantage over conventional formulations.

9 Summary of the Invention

10 It is an object of the stable, anticorrosive
11 concentrate and use-dilution microbicides in accordance with the
12 present invention to solve the problems outlined above that has
13 heretofore inhibited long-term storage and the anticorrosive
14 sterilization of surgical and dental instruments. These
15 improved microbicide solutions not only have the desired
16 stability but have been shown to have a significantly reduced
17 corrosive effect on certain metals than those of conventional
18 art mixtures of the peracetic acid/peroxide types known to the
19 applicants.

20 In accomplishing the foregoing objectives, there has
21 been provided in accordance with the present invention a stable,
22 anticorrosive to surgical and dental metals concentrate
23 including peracetic acid, acetic acid, hydrogen peroxide and
24 purified water mixed in a ratio of from about one to eleven
25 parts total acid to one part hydrogen peroxide. The new
26 concentrate has from substantially about .001 ppm to 200 ppm,
27 more preferably from about .001 ppm to 100 ppm, and most
28 preferably from about .001 ppm to 10 ppm of added stabilizers,
29 such as phosphonic acids, sodium pyrophosphates and from about
30 .001 - 10 ppm of ionic and non-ionic contaminants such as
31 divalent and trivalent ions, with no added surfactants, such as
32 ethoxylated decyl alcohols, sulfonate and sulfate types.

33 In accordance with another aspect of the present
34 invention, there has been provided a stable, anticorrosive to
35 surgical and dental metals use-dilution formulation including
36 a concentrate consisting essentially of at equilibrium peracetic
37 acid, acetic acid, hydrogen peroxide and an aqueous diluent,

1 said concentrate characterized in having from about .001- 200
2 ppm of added stabilizers, from about .001-10 ppm of ionic and
3 nonionic contaminants and no added surfactants; and a purified
4 aqueous diluent; wherein the concentrate is diluted in the
5 aqueous diluent from about 20 to 40 times.

6 In accordance with still another aspect of the present
7 invention, there has been provided a process for preparing a
8 sterilant concentrate as described above, including the steps of
9 introducing from about 17% by weight to about 40% by weight
10 hydrogen peroxide into a mixing drum, the hydrogen peroxide
11 having from about .001-200 ppm of added stabilizers; blending
12 thereinto from about 10% by weight to about 16% by weight acetic
13 acid; and adding a purified aqueous diluent having from about
14 .001-10 ppm of divalent and trivalent ions; wherein the
15 equilibrium concentration includes from about 16-38% by weight
16 hydrogen peroxide; from about 2.5-9% by weight acetic acid; from
17 about 1.5-6.0% by weight peracetic acid; and an aqueous diluent
18 and wherein the equilibrium concentration is characterized in
19 having from about .001-200 ppm of added stabilizers, from about
20 .001-10 ppm of ionic and nonionic contaminants and no added
21 surfactants.

22 One of the advantages of the present invention is that
23 the occasional allergic reactions of some individuals to the
24 conventional art formulations is reduced. Another advantage of
25 the present invention is that the presence of mineral-like
26 deposits from the use of the solutions of conventional art
27 formulations containing sequestrants or stabilizers is no longer
28 found. Perhaps most importantly, however, the present invention
29 allows metal instruments such as dental tools and surgical
30 instruments to be sterilized with significantly reduced
31 corrosivity as will be shown.

32 Further objects, features and advantages of the
33 present invention will become apparent from the detailed
34 description of the preferred embodiments, including the best
35 mode, which follow.

36
37

1 Brief Description of the Drawings

2 Figure 1 is a chart of stability of the concentrated
3 microbicide against time where the initial formulation contained
4 4.1% by weight of peracetic acid and the storage temperature was
5 at ambient temperature of 22°C;

6 Figure 2 is a chart of stability of concentrated
7 microbicide where the initial formulation contained 4.5% by
8 weight of peracetic acid and the storage temperature was 35°C;

9 Figure 3 is a chart of stability of the concentrated
10 microbicide against time where the initial formulation contained
11 4.2% by weight of peracetic acid and the storage temperature was
12 50°C;

13 Figure 4 is a chart of stability of the concentrated
14 microbicide against time where the initial formulation contained
15 23% by weight of hydrogen peroxide and the storage temperature
16 was 22°C;

17 Figure 5 is a chart of stability of the concentrated
18 microbicide against time where the initial formulation contained
19 23% by weight of hydrogen peroxide and the storage temperature
20 was 35°C;

21 Figure 6 is a chart of stability of the concentrated
22 microbicide against time where the initial formulation contained
23 23% by weight of hydrogen peroxide and the storage temperature
24 was 50°C;

25 Figure 7 is a chart of stability of the concentrated
26 microbicide against time where the initial formulation contained
27 23% by weight of hydrogen peroxide, 4% by weight of peracetic
28 acid and 8.4% acetic acid and the solution was stored at ambient
29 temperature;

30 Figure 8 is a chart of stability of the concentrated
31 microbicide against time where the initial formulation contained
32 23.8% by weight hydrogen peroxide and 4.47% by weight peracetic
33 acid and the solution was stored at ambient temperature;

34 Figure 9 is a chart of stability of the concentrated
35 microbicide against time where the initial formulation contained
36 23.8% by weight hydrogen peroxide and 4.47% peracetic acid and
37 the storage temperature was 35°C;

1 Figure 10 is a chart of stability of the concentrated
2 microbicide where the initial formulation contained 23.8% by
3 weight hydrogen peroxide and 4.47% by weight peracetic acid and
4 the storage temperature was 50°C;

5 Figure 11 is a chart of stability of the concentrated
6 microbicide where the initial formulation contained 17.2% by
7 weight hydrogen peroxide and 0.0% by weight peracetic acid and
8 the solution was stored at ambient temperature;

9 Figure 12 is a chart of stability of the concentrated
10 microbicide where the initial formulation contained 36.46% by
11 weight hydrogen peroxide and 0.0% by weight peracetic acid and
12 the solution was stored at ambient temperature;

13 Figure 13 is a chart of stability of the concentrated
14 microbicide where the initial formulation contained 27.4% by
15 weight hydrogen peroxide and 5.6% by weight peracetic acid and
16 the solution was stored at ambient temperature;

17 Figure 14 is a chart of stability of the concentrated
18 microbicide where the initial formulation contained 27.4% by
19 weight hydrogen peroxide and 5.3% by weight peracetic acid and
20 the solution was stored at 50°C.

21 Detailed Description of the Invention

22 Concentrate microbicide formulations in accordance
23 with the present invention possess the desirable property of a
24 long storage life without deleterious decomposition despite the
25 absence of conventional additions of stabilizers and
26 sequestrants as heretofore taught in the art. Additionally,
27 the concentrate compositions of the present invention are far
28 less corrosive to metals that are sterilized using the
29 compositions such as surgical and dental instruments. In
30 contrast with conventional art formulations containing added
31 surfactants, sequestrants and other stabilizers where visible
32 evidence of corrosion of the metals appeared in one or two
33 hours, formulations in accordance with the preferred embodiment
34 of the present invention visibly showed comparatively little
35 corrosion on the same metals during the same time period.

36 Manufacture of the preferred embodiment is effected by
37 mixing a solution of hydrogen peroxide with acetic acid diluted

1 with a purified aqueous diluent. The hydrogen peroxide is
2 selected from commercially available sources having low
3 concentrations of stabilizers, preferably .001 ppm to 200 ppm,
4 more preferably from about .001 ppm to 100 ppm, and most
5 preferably from about .001 ppm to 15 ppm of added stabilizers,
6 such as phosphonic acids, sodium pyrophosphates. Sources of
7 such hydrogen peroxide are available from FMC Corporation
8 (Philadelphia, PA).

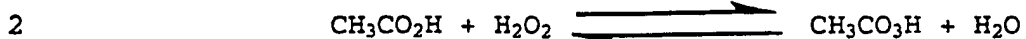
9 In addition, the preferred embodiment in accordance
10 with the present invention preferably includes no contaminants.
11 Contaminants such as divalent and trivalent ions, principally,
12 iron, manganese, magnesium, nickel and cobalt, and undesirable
13 trace organics found in the manufacturing process, principally,
14 surfactants, acetone, methanol, ethanol, which are typically
15 present in conventional art formulations are found in the
16 present invention in amounts preferably from about 5-10 ppm and
17 most preferably from about .001-5 ppm in the final composition.

18 Referring to Table I, the preferred composition is
19 shown.

TABLE I

	Initial Mixture	After Equilibrium
21 H ₂ O ₂	17-40% by wt.	16-38% by wt.
22 HOAc	10-16% by wt.	2.5-9.0% by wt.
23 HOOAc	0	1.5-6.0% by wt.

24 The concentrate microbicide in accordance with the
25 present invention may be formulated over a wide range of
26 concentrations of the active materials. After equilibrium the
27 concentrate microbicide may have as high as 38% by weight
28 hydrogen peroxide at equilibrium with the peracetic acid
29 concentration ranging from 1.5% to 6.0% as indicated in Table 1.
30 Since the concentrate when initially mixed contains no peracetic
31 acid and therefore is not used immediately, it is stored for
32 approximately 19-20 days until the solution equilibrates and
33 peracetic acid is formed by the reaction of hydrogen peroxide
34 with acetic acid as illustrated in Reaction 1.
35
36
37

1 Reaction 1.

3 The concentrate manufactured in accordance with the
4 present invention is stored and shipped in amber colored plastic
5 bottles that have been thoroughly precleaned with purified water
6 to ensure no heavy metal contamination. Stability studies were
7 run at ambient (22°C), 35°C and 50°C to determine the stability
8 of the concentrate over time at these temperatures. Data
9 regarding the relative stability of H₂O₂ and HOOAc in the
10 concentrate composition and the concentrate itself are shown in
11 Figures 1-14. Acetic acid typically was not measured for
12 stability since it is not one of the active ingredients of the
13 concentrate composition; in other words, acetic acid has no
14 microbicidal activity. As can be seen from Figures 1-15, the
15 solutions were very stable.

16 In addition to stability studies, corrosivity studies
17 were run on the concentrate compositions, the results of which
18 may be seen by referring to Table IIA. Table IIB details the
19 results of the corrosivity run on conventional art formulations
20 while Table IIC details the results of corrosivity testing on
21 the component parts of the conventional art formulation. Table
22 IID details the results of corrosivity studies run on the use-
23 dilution formulations of the conventional art and several of the
24 preferred embodiments of the present invention.

25 Corrosivity studies were done using a variety of metal
26 coupons. They included naval brass 464 and aluminum 5052. The
27 coupons are commercially available from Metal Samples Company
28 (Munford, Al.)

29 Coupons were cleaned by the following methods to
30 remove all foreign debris and to ensure accurate results. Brass
31 coupons were placed on edge in a 50% by weight solution of HCl
32 for two minutes at ambient temperature. Aluminum coupons were
33 placed on edge in concentrated nitric acid for three minutes at
34 ambient temperature. During all phases of the testing, coupons
35 were handled by gloved laboratory personnel to insure that the
36 coupons were not exposed to any foreign materials prior to

1 placing them in the test solutions. All coupons are stamped with
 2 a number to aid in identification. All coupons were air dried
 3 under a ventilated hood and weighed prior to testing on a
 4 Mettler AE 100 analytical balance. The weight was recorded as
 5 the initial weight.

6 The exposure time of the coupons was .5 hours for
 7 brass and 5 hours for aluminum when testing the concentrate
 8 microbicide and 5 hours for brass and 1 week for aluminum when
 9 testing the use-dilution formulation of the microbicide. The
 10 coupons were tested in the test solutions indicated below at
 11 ambient temperature.

12 Solution volumes of 70ml were dispensed into plastic
 13 disposable cups. The coupons were allowed to remain in solution
 14 for the times indicated above. After the time period had
 15 expired, the solution was discarded and the coupons were placed
 16 to dry, without rinsing, standing on edge in a ventilating hood.
 17 After drying for 30-60 minutes, the coupons were re-weighed.
 18 The difference between the initial weight and final weight (W)
 19 was used to calculate the corrosion rate as follows:

$$20 \quad \text{Corrosion rate (mm/yr)} = \frac{(K \times W)}{(A \times T \times D)} \quad \text{where:}$$

21
 22 $K = \text{a constant } (8.76 \times 10^{-4})$

23 $T = \text{time of exposure in hours}$

24 $A = \text{area in cm}^2 \text{ (28.7 cm}^2\text{)}$

25 $W = \text{weight loss in grams (initial weight - final weight)*}$

26 *To correct for possible weight loss due to product
 27 removal, a "blank" coupon was weighed, cleaned by the
 28 procedure indicated above and weighed again.

29 $D = \text{density in g/cm}^3$ **

30 **Brass = 8.41 g/cm³

31 Aluminum 5052 = 2.68 g/cm³

32

33 TABLE IIA

34 Titration

35 <u>Samples</u>	<u>H₂O₂</u>	<u>PAA</u>	<u>HoAc</u>
36 1	38.8%	4.54%	2.88%
37 2	34.8%	4.23%	3.27%

1	3	27.6%	5.0%	6.1%
2	4	27.4%	5.4%	6.2%
3	5	27.3%	5.5%	5.7%
4	6	27.55%	5.03%	6.06%
5	7	27.4%	5.4%	6.21%
6	8	27.34%	5.51%	5.68%
7	9	27.2%	5.72%	6.67%
8	10	27.2%	5.70%	6.82%
9	11	27.0%	5.62%	6.66%
10	12	27.0%	4.00%	5.71%
11	13	26.5%	4.14%	6.50%
12	14	22.5%	4.19%	7.84%
13	15	22.5%	3.91%	8.1%
14	16	22.5%	3.86%	8.1%
15	17	19.6%	2.68%	8.62%
16	18	16.9%	1.66%	6.26%

17

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Corrosion

19	<u>Samples</u>	<u>Brass</u>	<u>Aluminum</u>
20	1	19.9 mm/yr	0.012 mm/yr
21	2	33.3 mm/yr	.006 mm/yr
22	3	52.02 mm/yr	.284 mm/yr
23	4	58.91 mm/yr	.024 mm/yr
24	5	52.07 mm/yr	.022 mm/yr
25	6	52.02 mm/yr	.283 mm/yr
26	7	58.91 mm/yr	.023 mm/yr
27	8	58.07 mm/yr	.020 mm/yr
28	9	57.56 mm/yr	.010 mm/yr
29	10	54.53 mm/yr	.376 mm/yr
30	11	49.96 mm/yr	.013 mm/yr
31	12	82.10 mm/yr	.001 mm/yr
32	13	93.70 mm/yr	.018 mm/yr
33	14	95.62 mm/yr	1.320 mm/yr
34	15	93.25 mm/yr	.153 mm/yr
35	16	93.20 mm/yr	.230 mm/yr
36	17	45.3 mm/yr	.257 mm/yr
37	18	43.4 mm/yr	.173 mm/yr

Table IIBConventional Art FormulationTitration

	<u>H₂O₂</u>	<u>PAA</u>	<u>HoAc</u>	<u>Phosphonic Acid</u> <u>Stabilizer</u>
<u>Samples</u>				
19	22.4%	3.96%	8.27%	1.0%
20	21.0%	4.3%	9.86%	1.0%

Corrosivity

<u>Samples</u>	<u>Brass</u>	<u>Aluminum</u>
19	295.50 mm/yr	121.63 mm/yr
20	295.48 mm/yr	121.65 mm/yr

Table IICCorrosivity of Component Parts

<u>Samples</u>	<u>Brass</u>	<u>Aluminum</u>
1% stabilizer	.586 mm/yr	.367 mm/yr
22.7% H ₂ O ₂	.528 mm/yr	.316 mm/yr
10.2% HoAc	.160 mm/yr	.167 mm/yr

Table IIDUse-dilution Formulations*

<u>Conventional Art</u>	<u>Brass</u>	<u>Aluminum</u>
3% Sample 19	23.63 mm/yr	0.820 mm/yr
3% Sample 20	23.84 mm/yr	0.747 mm/yr

Present Invention

<u>Sample X</u> [27% H ₂ O ₂ , 5.3% PAA, 5.5% Ac]	12.77 mm/yr	0.437 mm/yr
<u>Sample Y</u> [37% H ₂ O ₂ , 4.8% PAA, 2.2% Ac]	5.39 mm/yr	0.374 mm/yr
<u>Sample Z</u> [22% H ₂ O ₂ , 4.0% PAA, 7.0% Ac]	14.63 mm/yr	0.441 mm/yr

* All use-dilution samples were prepared using 3% of the concentrate formula diluted in a purified aqueous diluent.

1 In the present preferred form of the invention, the
2 concentrate is shipped in a small quantity in an amber colored
3 plastic bottle together with a gallon of purified deionized
4 water. Before use, the concentrate of the preferred embodiment
5 is diluted from about 20 to 40 times, more preferably from about
6 25 to 35 times, and most preferably from about 30 to 33 times
7 with a purified aqueous diluent prepared as described below.
8 This results in a use-dilution formulation of approximately 3.0%
9 to 4.5% by volume of concentrate. Ordinary tap water is
10 generally unsuitable as a diluent because of contaminants, such
11 as divalent and trivalent ions, contained therein. If ordinary
12 tap water is used to dilute the concentrate, the shelf life of
13 the use-dilution formulation will likely be less than when the
14 purified aqueous diluent is used and corrosivity will increase
15 as the purity of the water decreases. The recommended shelf
16 life of the use-dilution microbicide is seven days.
17 Consequently, it may be used for several applications or reused
18 several times during that period of time with no change in the
19 stability or in the anticorrosive or sporicidal activity.

20 A purified aqueous diluent suitable for use in the
21 concentrate and use-dilution formulation in accordance with the
22 present invention is prepared in the following manner. Raw city
23 water is passed through an activated carbon bed containing 10
24 cubic feet of carbon in a 24 in. diameter fiberglass tank with a
25 2 in. diameter super flow head and a 2 in. diameter distributor.

26 The water is then passed through softening beds well
27 known in the art of water purification to remove calcium
28 chloride and magnesium. Suitable softening beds are available
29 from Eco Water Systems (Woodbury, MN). The water is then passed
30 through a one micron polypropylene cloth sediment filter having
31 an efficiency rate of 93%. The cloth filter catches any
32 particulate matter remaining in the water that has a size
33 greater than 1_{μ} .

34 The water then flows through an eight inch diameter
35 reverse osmosis membrane filter. The membrane filter is made
36 from a spirally wound polyamide sheet membrane and is
37 commercially available as Model No. BW-30 from Filmtec Co.

1 (Edina, MN). The water effluent has less than 5 ppm dissolved
2 solids.

3 After the water is treated by passing it through the
4 reverse osmosis membrane, it is circulated through an
5 ultraviolet disinfection unit. The unit employs dual wave
6 lengths at 185nm and 254nm and is rated at 99%.9 bacterial
7 reduction. A suitable commercially available unit is the
8 Aquafine U.V. Water Sterilizer, CLS-4R (Aquafine Corp, Valencia,
9 CA.)

10 Post-UV light treatment, the water flows through an
11 anion exchange resin bed and a cation exchange resin bed. The
12 anion exchange resin bed is a strongly basic anion exchange
13 resin based on a styrenedivinylbenzene copolymer matrix. Its
14 exchange capacity is derived from the $N \cdot (CH_3)_2H_4OH$
15 (dimethylethanolamine) group. Anion exchange resin bed capable
16 of purifying the aqueous diluent in accordance with the present
17 invention may be purchased from Sybron Chemicals Inc
18 (Birmingham, N.J.) under the trade name IONAC ASB-2. The cation
19 exchange resin bed is a bead-form, standard crosslinked,
20 polystyrene sulfonate cation exchange resin with a capacity of
21 1.4 mEq/ml for further demineralization. Treated water is
22 stored in a 1000-5000 gallon tank. Resistivity is constantly
23 measured and maintained at 17-17.5 mOhms.

24 Prior to using the above manufactured water in the
25 concentrate mixtures or use-dilution formulations in accordance
26 with the present invention, the water is tested for pyrogen,
27 yeast, molds and bacteria by the following methods.

28 Pyrogen Testing. Five milliliters of sterile water is
29 pipetted into a vials of endotoxin, commercially available as
30 endotoxin from E. coli strain 055.B5 from Whittaker Bioproducts,
31 Inc. (Walkersville, MD). Five and two-tenths milliliters of
32 sterile water is pipetted into a vial of lysate, commercially
33 available as Pyrogen T from Whittaker Bioproducts. One hundred
34 lambda of the reconstituted lysate is then pipetted into
35 disposable conical tubes. The diluted lysate has a sensitivity
36 of 0.06 endotoxin units.

37

11 Yeast, Molds and Bacteria Testing

28

30 All mixing drums and tanks were thoroughly cleaned
31 using purified water. Sixty percent by weight of purified water
32 was added to a cleaned mixing tank at ambient temperature.
33 Bacterial testing and yeast and molds testing of the water used
34 in manufacturing the concentrate was reported as 0 colony
35 forming units per five milliliters of sample for both tests. An
36 air driven drum pump was turned on to start recirculation of the
37 batch. Fourteen percent by weight of acetic acid was added to

1 the mixing tank containing the deionized water. After the
2 acetic acid was added, the batch was covered and recirculated
3 for one hour. Using an air driven drum pump, 26% by weight of
4 hydrogen peroxide was added into the mixing tank and the cover
5 replaced. The composition was recirculated for two hours after
6 all chemicals were added. After two hours, the recirculating
7 pump was stopped. The concentrate was dispensed into clean 55
8 gallon drums for storage and equilibrated for 19 days. After 19
9 days from the production date, a sample was taken from the
10 concentrate batch and the concentration was determined to be
11 22.5% H₂O₂, 3.96% peracetic acid, and 8.1% acetic acid.

12 Microbicidal Effectiveness

13 A 3.0% solution of the concentrate microbicide
14 manufacture in Example 1 was tested for sporicidal activity
15 according to the methods outlined in the Official Methods of
16 Analysis of the Association of Official Analytical Chemists (K.
17 Helrich 15th ed. 1990) (966.04 pp. 141-142), the text of which
18 is hereby specifically incorporated by reference.

19 Briefly, cultures of two sporeformer organisms,
20 *Bacillus subtilis* ATCC 19659 and *Clostridium sporogenes* ATCC
21 3584 were grown in the appropriate medium. Each organism was
22 used to contaminate two types of carriers, namely, silk suture
23 and porcelain penicylinders. The carriers were dried for a
24 minimum of 24 hrs. under vacuum. Carriers were tested for acid
25 resistance and viability. Five carriers were placed in test
26 tubes containing 10 mL. of test solution, and exposed for 30
27 min. at 50°C. Following contact, carriers were neutralized in
28 thioglycollate medium and incubated for 21 days at 37°C. If no
29 growth was observed after 21 days, the test tubes were heat
30 shocked for 20 minutes at 80°C to activate any remaining spores
31 and incubated for 72 hrs. at 37°C. For chemical sterilant
32 claims, no survival of any organism/spore can be tolerated for
33 qualification of the solution by the U.S. Environmental
34 Protection Agency as a sterilant. The results of the sporicidal
35 testing of the concentrate microbicide in accordance with the
36 microbicide prepared in Example 1 are as follows:

1	Lot	Org. Carrier	Titer	Resistance	#Survivors/ #Tested
2					
3	2M004	Cl.sp. Suture	10 ⁻⁶	20 min.	0/60
4	2M004	Cl.sp. Cylinder	10 ⁻⁵	5 min.	0/60
5	2M004	B. sub.suture	10 ⁻⁴	20 min.	0/60
6	2M004	B. sub.Cylinder	10 ⁻⁴	2 min.	0/60
7					

8 The results of the AOAC procedure reference test shows that
9 the microbicide of the invention, in addition to being stable,
10 is effective as a sterilant.

11 Corrosivity of the solution of Example 1 was tested.
12 The results appear as Sample 15 in Table IIA.

13

14 Example 2

15 All mixing drums and tanks were thoroughly cleaned
16 using purified water. 23.3% by weight of purified water was
17 added to a cleaned mixing tank at ambient temperature.
18 Bacterial testing and yeast and molds testing of the water used
19 in manufacturing the concentrate was reported as 0 colony
20 forming units per five milliliters of sample for both tests. An
21 air driven drum pump was turned on to start recirculation of the
22 batch. 16.7% by weight of acetic acid was added to the mixing
23 tank containing the purified water. After the acetic acid was
24 added, the batch was covered and recirculated for one hour.
25 Using an air driven drum pump, 40.0% by weight of hydrogen
26 peroxide was added into the mixing tank and the cover replaced.
27 The composition was recirculated for two hours after all
28 chemicals were added. After two hours, the recirculating pump
29 was stopped. The concentrate was dispensed into clean 55 gallon
30 drums for storage. After 19 days from the production date, the
31 batch was adjusted to a hydrogen peroxide level of 36.5% and a
32 peracetic acid level of 4.5% by adding water and hydrogen
33 peroxide. The solution was allowed to equilibrate for an
34 additional 33 days. A sample was taken from the concentrate
35 batch and the concentration was determined to be 36.65% hydrogen
36 peroxide, 4.31% peracetic acid and 2.88%.

37

1 The results of the sporicidal testing of a 3% solution
 2 of the concentrate microbicide in accordance with the
 3 microbicide prepared in Example 2 are as follows:

4 Lot	Org. Carrier	Titer	Resistance	#Survivors/ #Tested
5				
6 2008-2a	Cl.sp. Suture	10 ⁻⁶	20 min.	0/60
7 2008-2a	Cl.sp. Cylinder	10 ⁻⁶	10 min.	0/60
8 2008-2a	B. sub.suture	10 ⁻⁴	10 min.	0/60
9 2008-2a	B. sub.Cylinder	10 ⁻⁴	2 min.	0/60

10

11 The concentrate prepared in accordance with Example 2
 12 was tested for corrosivity. The results are shown in Table IIA
 13 as Sample 2.

14 Example 3

15 Using the method set forth in Examples 1 and 2, 7.74%
 16 by weight purified water was added to 17.12% by weight H₂O₂ and
 17 8.143% by weight HOAc. Bacterial testing and yeast and molds
 18 testing of the water used in manufacturing the concentrate was
 19 reported as 0 colony forming units per five milliliters of
 20 sample for both tests. After mixing for the specified time
 21 periods, the concentrate was allowed to stand for 19 days and a
 22 sample was taken to determine the content of H₂O₂ and HOOAc.

23 The final concentration was determined to be 16.86% by weight
 24 H₂O₂, 1.66% peracetic acid and 6.26% acetic. The solution was
 25 found to have microbicidal activity as follows:

26 Lot	Org. Carrier	Titer	Resistance	#Survivors/ #Tested
27				
28 2028-1	Cl.sp. Suture	10 ⁻⁵	10 min.	0/60
29 2028-1	Cl.sp. Cylinder	10 ⁻⁶	10 min.	0/60
30 2028-1	B. sub.suture	10 ⁻⁴	10 min.	0/60
31 2028-1	B. sub.Cylinder	10 ⁻⁴	2 min.	0/60

32

33 Corrosivity was tested and the results are detailed in
 34 Table IIA as Sample 18.

35 While the preceding compositions in accordance with
 36 the invention are the preferred form it is to be understood that
 37 concentrate formulations may be within the ranges given and

- 1 still provide the advantages of the invention. Those skilled in
- 2 the art may recognize other equivalents to the specific
- 3 embodiments described herein which equivalents are intended to
- 4 be encompassed by the appended claims.

1 We claim:

- 2 .1. A stable, anticorrosive to surgical and dental
3 metals concentrate consisting essentially of at equilibrium
4 peracetic acid, acetic acid, hydrogen peroxide and an aqueous
5 diluent, said concentrate characterized in having from about
6 .001-200 ppm of added stabilizers, from about .001-10 ppm of
7 ionic and nonionic contaminants and no added surfactants.
- 8 2. The concentrate in accordance with Claim 1
9 wherein the concentration of added stabilizer is from about .001-
10 100 ppm.
- 11 3. The concentrate is accordance with Claim 1
12 wherein the concentration of added stabilizer is from about .001-
13 10 ppm.
- 14 4. The concentrate of Claim 1 wherein the
15 equilibrium composition comprises:
- 16 a) H_2O_2 16 to 38% by weight;
17 b) HOAc 2.5 to 9.0% by weight;
18 c) HOOAc 1.5 to 6.0% by weight; and
19 d) the balance is a purified aqueous diluent.
- 20 5. The concentrate in accordance with Claim 4
21 wherein the concentration of added stabilizer is from about .001-
22 100 ppm.
- 23 6. The concentrate in accordance with Claim 4
24 wherein the concentration of added stabilizer is from about .001-
25 10 ppm.
- 26 7. The concentrate in accordance with Claim 1
27 wherein the equilibrium concentration comprises:
- 28 a) H_2O_2 23 to 24% by weight;
29 b) HOAc 9 to 10% by weight;
30 c) HOOAc 4 to 6% by weight; and
31 d) the balance is a purified aqueous diluent.
- 32 8. The concentrate in accordance with Claim 7
33 wherein the concentration of added stabilizer is from about .001-
34 100 ppm.
- 35 9. The concentrate in accordance with Claim 7
36 wherein the concentration of added stabilizer is from about .001-
37 10 ppm.

1 10. A method of formulating a stable, anticorrosive
2 to surgical and dental metals concentrate microbicide comprising
3 the steps of:

4 a) blending hydrogen peroxide, acetic acid and a
5 purified aqueous diluent to result in a solution which at
6 equilibrium has from about .001-200 ppm added stabilizers, from
7 about .001-10 ppm of ionic and nonionic contaminants and no
8 added surfactants.

9 11. A method of formulating a stable, anticorrosive
10 to surgical and dental metals concentrate microbicide comprising
11 the steps of:

12 a) introducing from about 17% by weight to about 40%
13 by weight hydrogen peroxide into a mixing drum, said hydrogen
14 peroxide having from about .001-200 ppm of added stabilizers;
15 and

16 b) blending thereinto from about 10% by weight to
17 about 16% by weight acetic acid; and

18 c) adding a purified aqueous diluent having from about
19 .001-10 ppm of divalent and trivalent ions;
20 wherein the equilibrium concentration comprises:

21 i) from about 16-38% by weight hydrogen peroxide;

22 ii) from about 2.5-9% by weight acetic acid;

23 iii) from about 1.5-6.0% by weight peracetic acid;

24 and

25 iv) an aqueous diluent

26 wherein said equilibrium concentration is characterized in
27 having from about .001-200 ppm of added stabilizers, from about
28 .001-10 ppm of ionic and nonionic contaminants and no added
29 surfactants.

30 12. A stable, anticorrosive to surgical and dental
31 metals use-dilution microbicide comprising:

32 a) a concentrate consisting essentially of at
33 equilibrium peracetic acid, acetic acid, hydrogen peroxide and
34 an aqueous diluent, said concentrate characterized in having
35 from about .001- 200 ppm of added stabilizers, from about .001-
36 10 ppm of ionic and nonionic contaminants and no added
37 surfactants; and

38 b) a purified aqueous diluent;

39

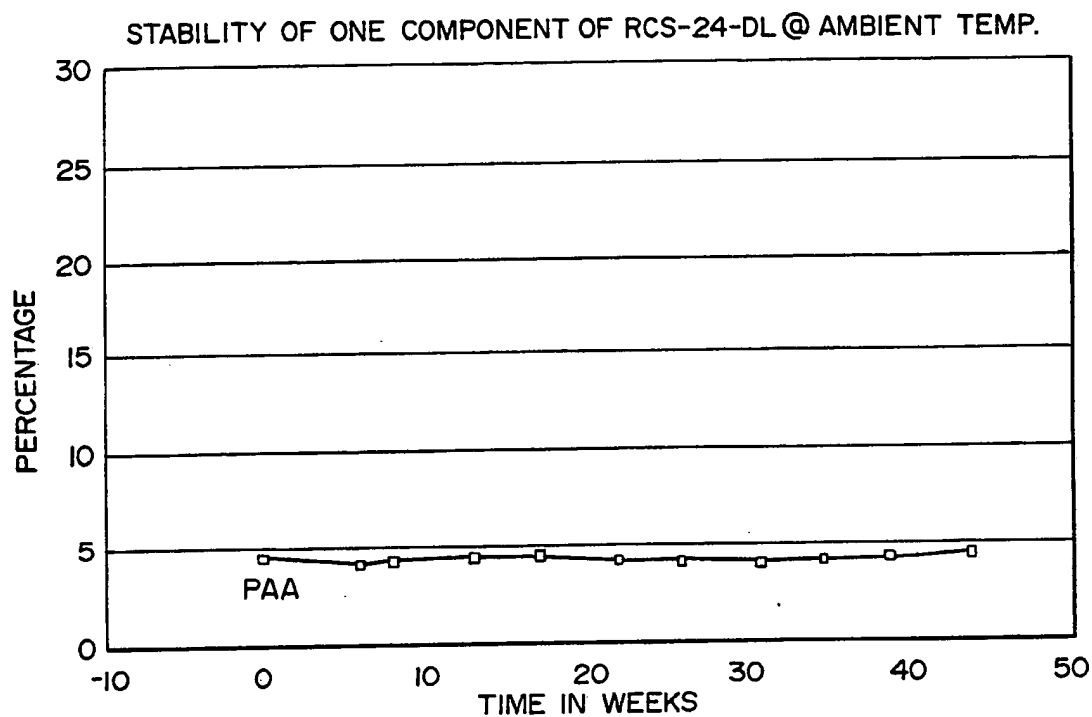
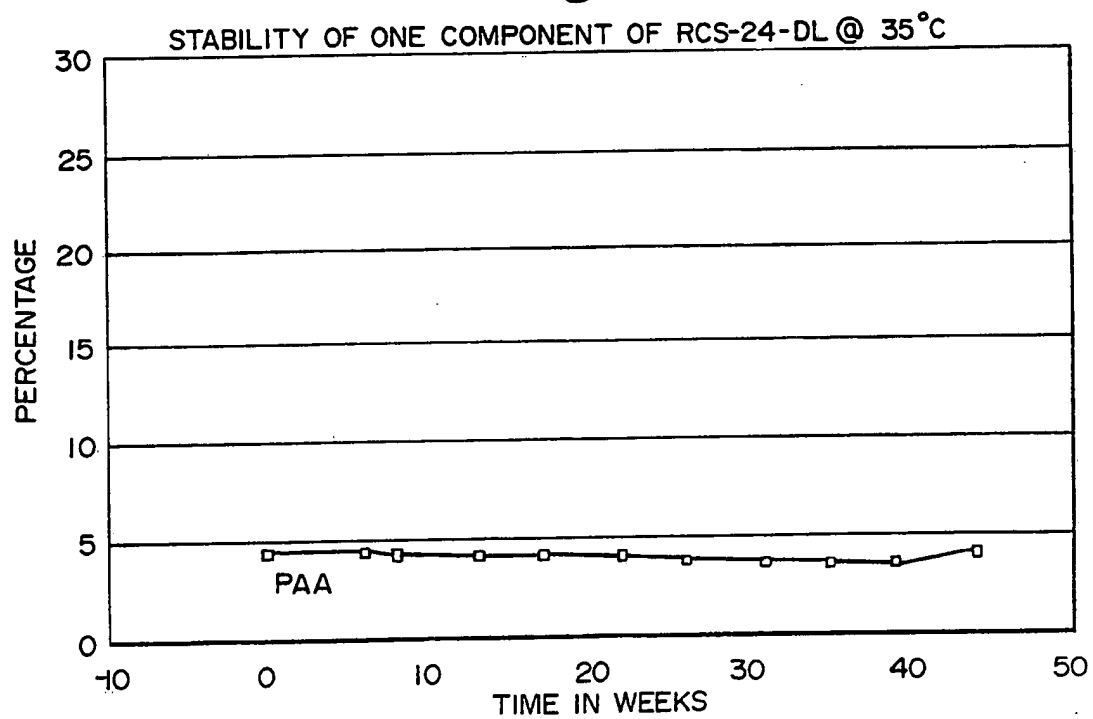
1 wherein said concentrate is diluted in said aqueous diluent from
2 about 20 to 40 times.

3

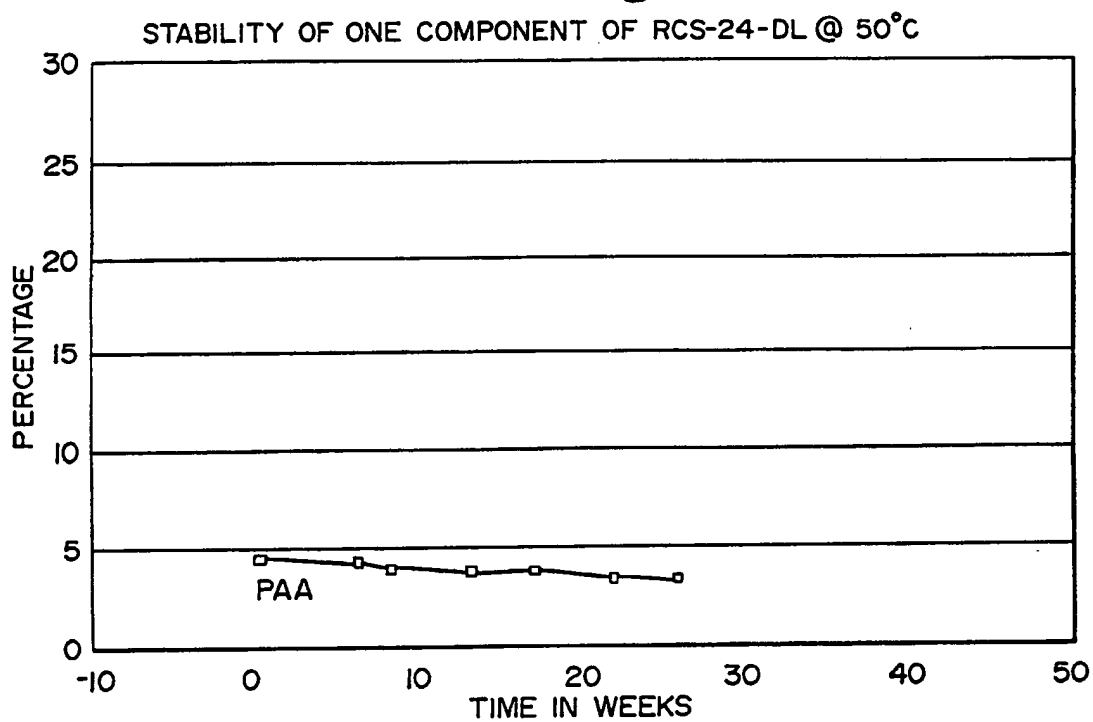
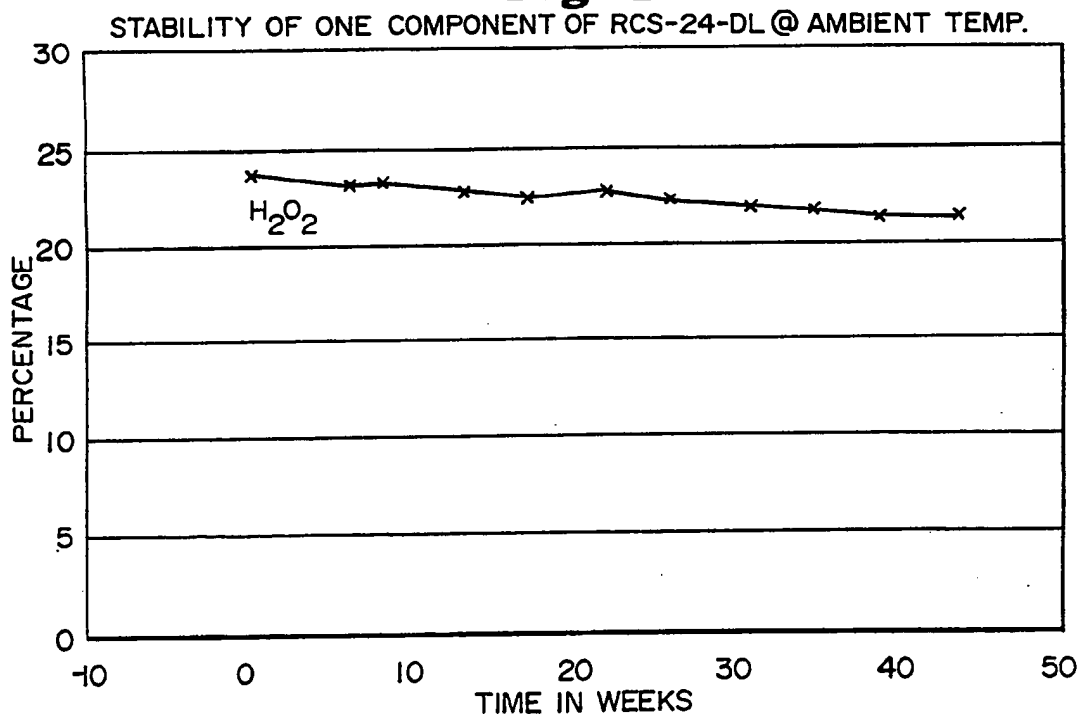
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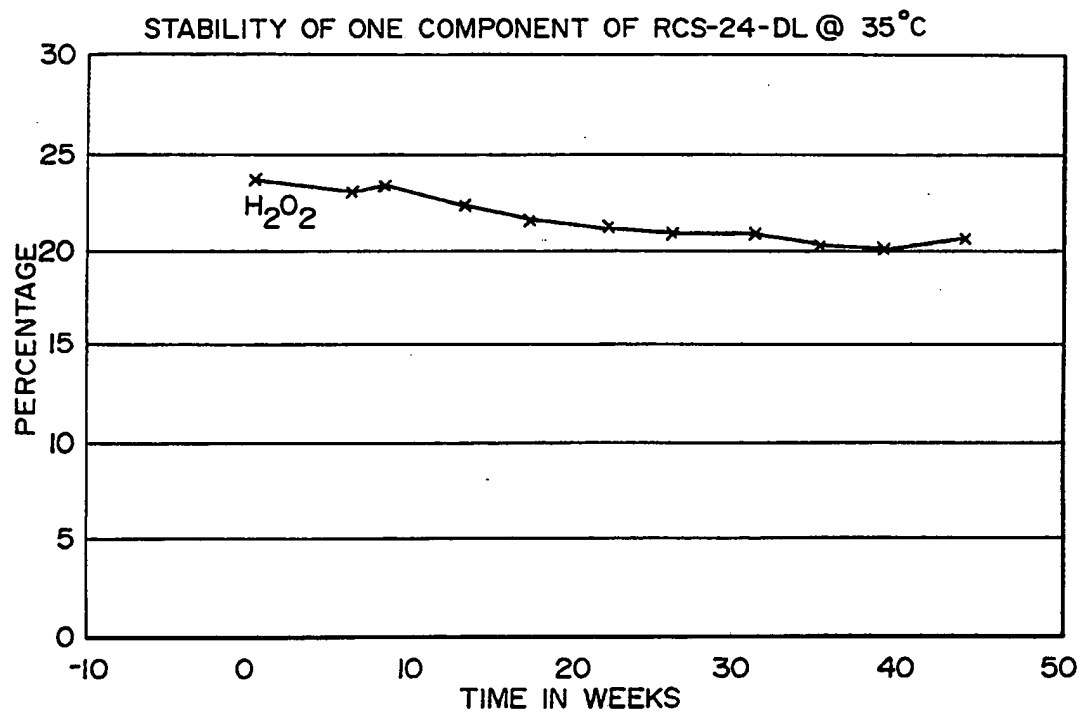
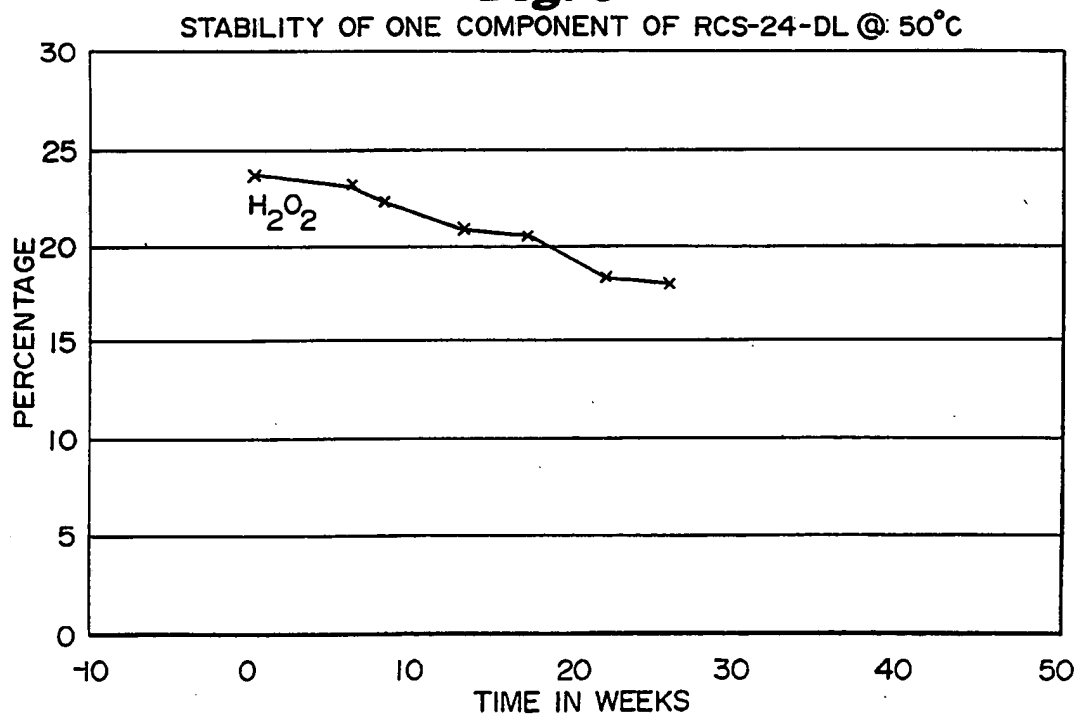
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Fig. 1**Fig. 2**

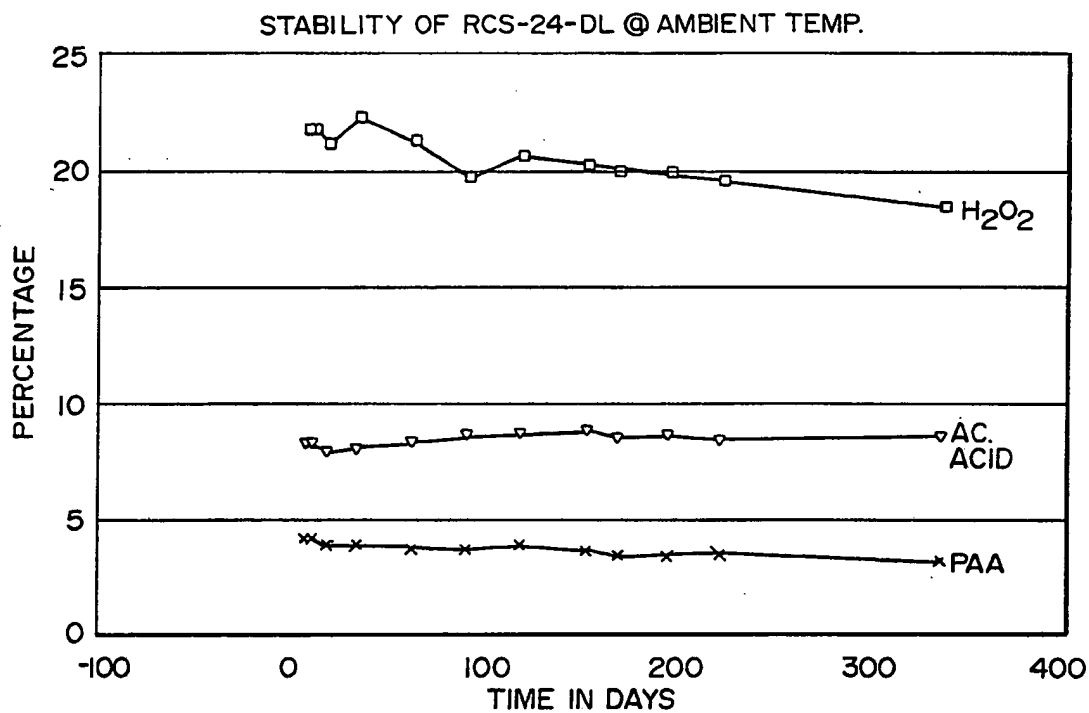
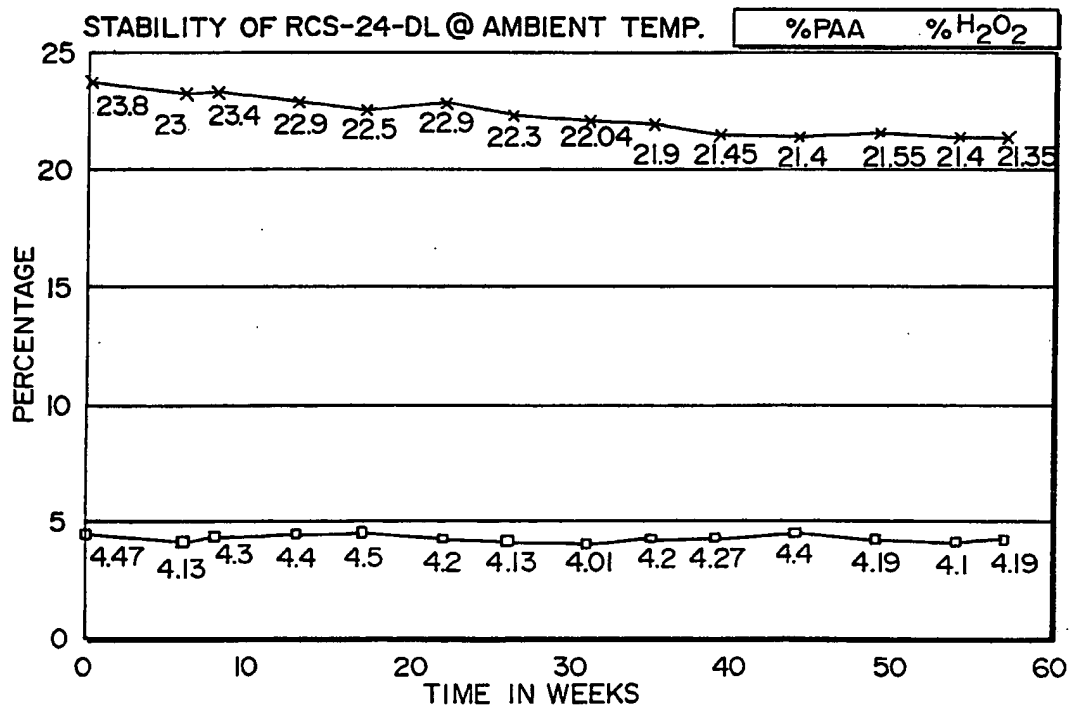
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Fig. 3**Fig. 4**

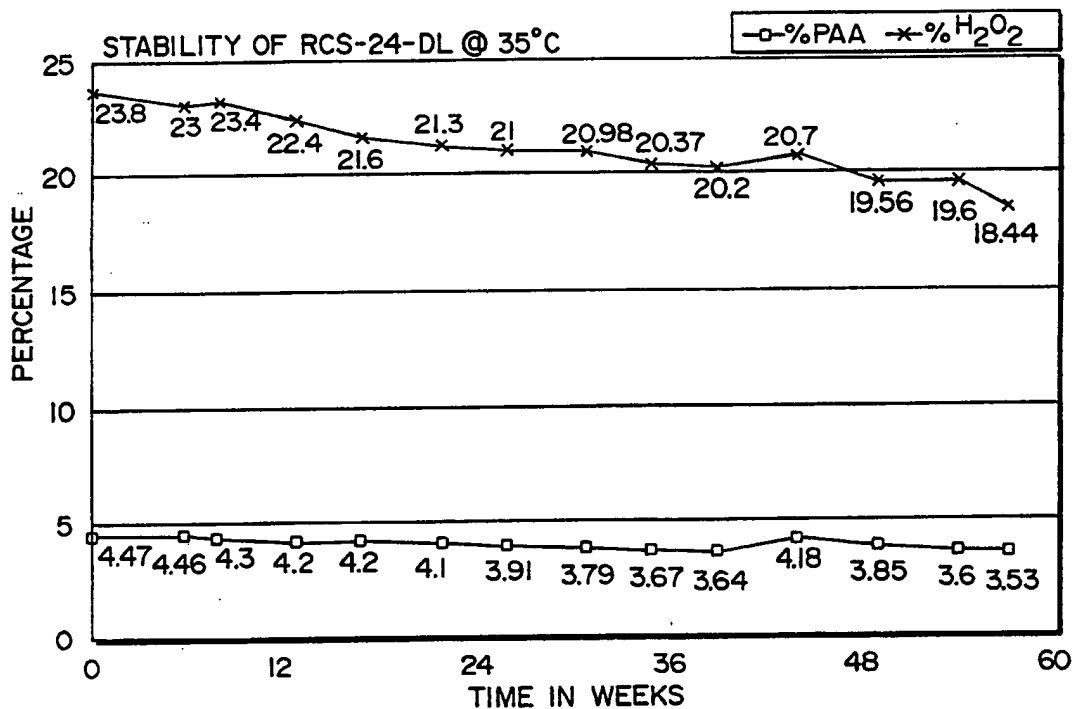
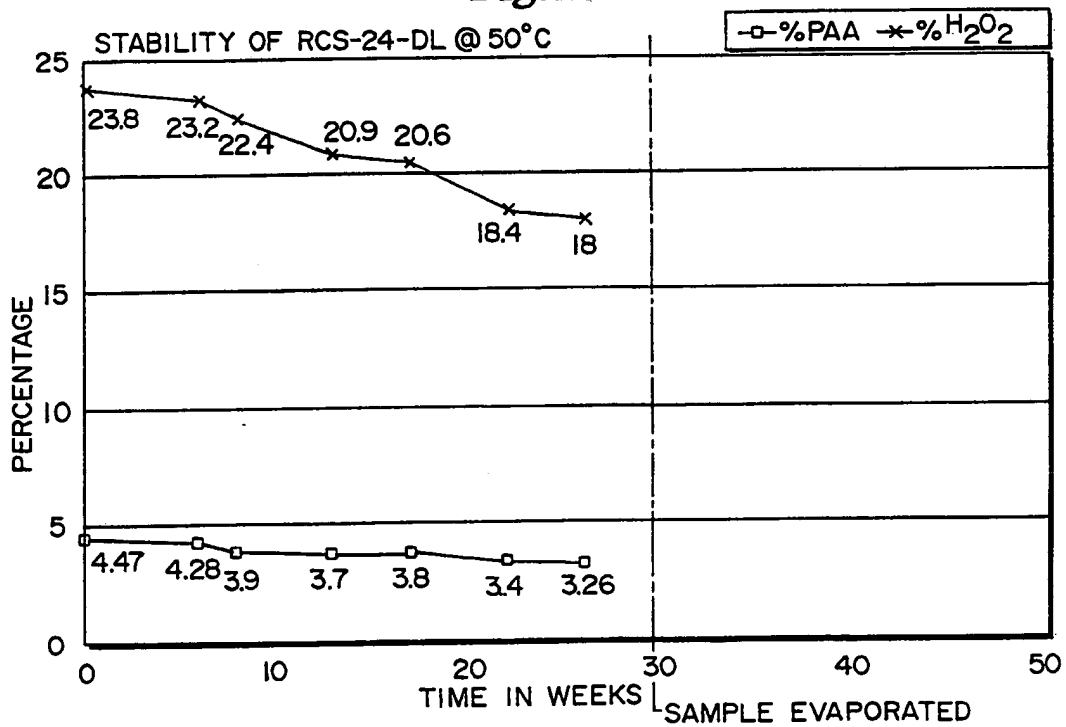
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Fig. 5**Fig. 6**

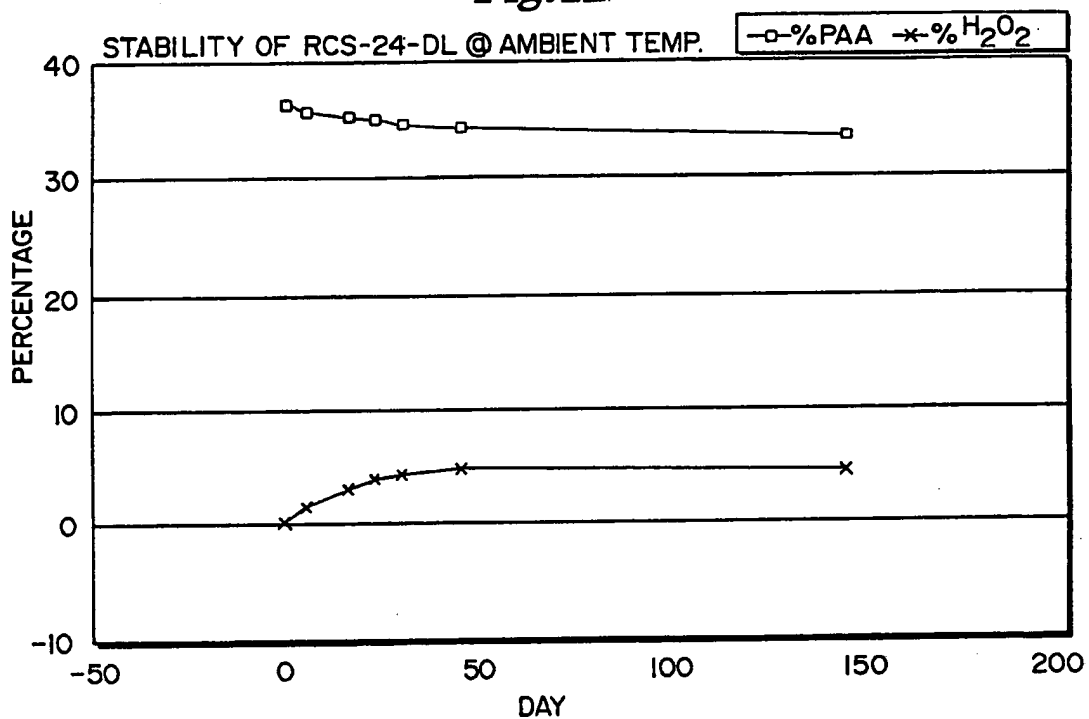
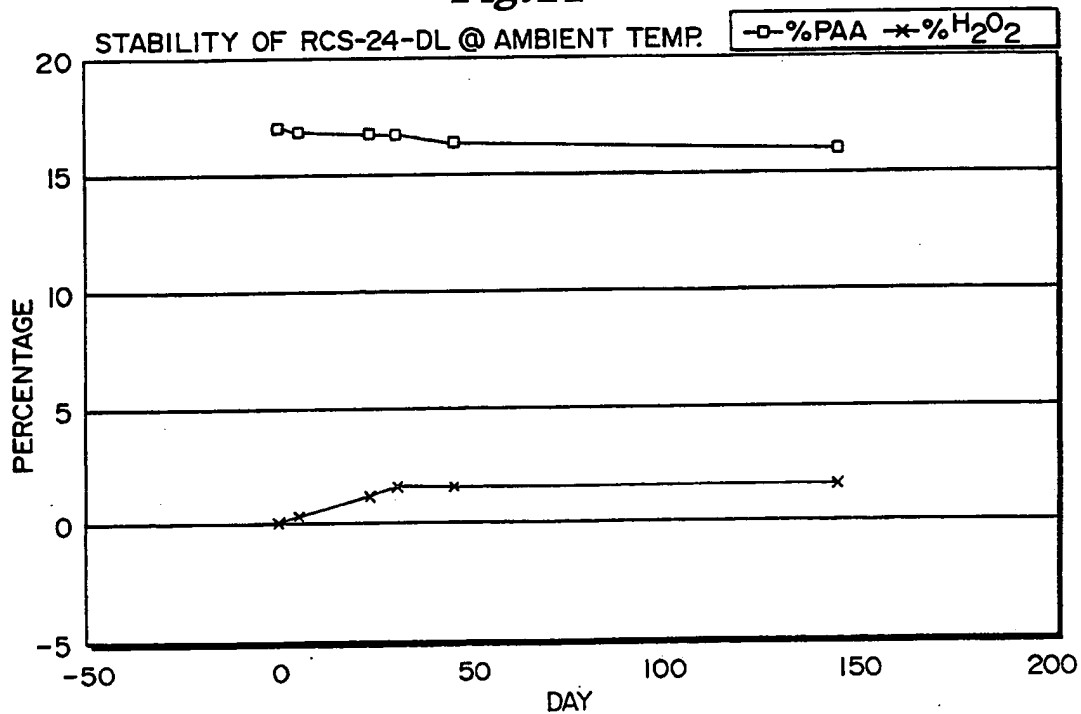
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Fig.7*Fig.8*

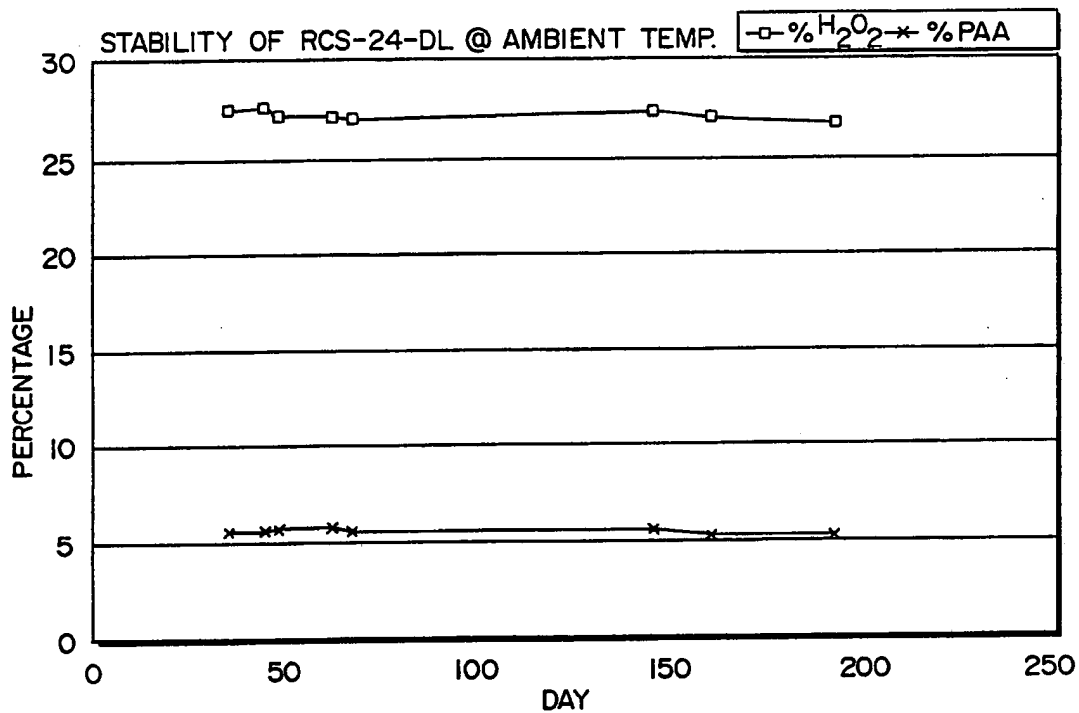
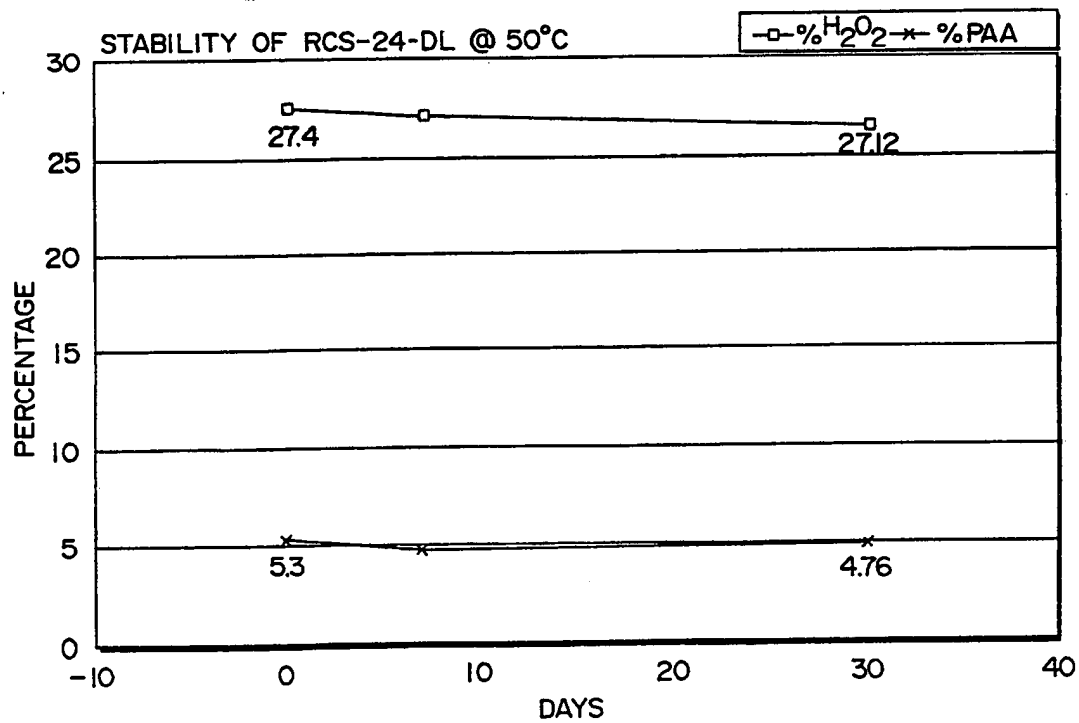
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Fig.9*Fig.10*

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Fig.12*Fig.11*

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Fig.13*Fig.14*

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US92/05877

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 33/40; A61K 31/19

US CL :424/616; 514/55

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. :

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Chemical Abstract, volume 110, NO. 22 issued 29 May 1989. L. COSENTINO, "Stable microbicides containing hydrogen peroxide and acetic acid and peracetic acid". See abstract No. 199231u.	1-12

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be part of particular relevance	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z*	document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means		
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Date of the actual completion of the international search 21 OCTOBER 1992	Date of mailing of the international search report 11/1992
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